DOI: 10.1002/alz.056499

BASIC SCIENCE AND PATHOGENESIS

POSTER PRESENTATION

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

A study on the distribution of *Porphyromonas gingivalis* repeated epitope in hemagglutinin/adhesion and hagA gingipains domain antigen and DNA in Alzheimer brains

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Abstract

Background: Alzheimer's disease (AD) is a progressive neuroinflammatory and neurodegenerative disease of the brain, defined by the accumulation and deposition of beta-amyloid, which has recently been identified as an antimicrobial peptide suggesting an infectious etiology. Specific bacterial infections and factors especially caused by the oral Keystone Pathogen-Porphyromonas gingivalis (Pg) in both humans and animal models have shown to initiate and chronically stimulate the systemic innate host defense systems and inflammasome. Overtime these compromise the integrity of the blood brain barrier, localize in the brain parenchyma neurons and supporting cells and through multiple inflammatory pathways and lead to activation of microglia and astrocytes.

Method: A novel anti-pg bacterial monoclonal antibody currently in pre- and clinical development was used for all described work. Forty-six brain tissue samples (frontal and temporal biopsies) from 23 brain specimens (7 AD and 16 AMC) were subjected to PCR-based liquid hybridization assay to detect *P. gingivalis* DNA. All were negative for *P. gingivalis* DNA. Alzheimer brain sections from multiple functionally distinct anatomic regions and 15 different patient choroid plexus were tested by Porphyromonas gingivalis antigen-specific immuno-histochemistry.

Result: A unique Pg clinically relevant antigen was detected by IHC in multiple functionally distinct brain sections from all AD brains tested. This antigen was found with greatest intensity and frequency in the Fronto-temporal, Hippocampal lobes, Choroid plexus, Occipital and Cerebellar lobes. No P.g. DNA was found by PCR in 7 different AD brains with 46 different tissue samples from the frontal and temporal lobes. Three AD brains tested for both DNA and the novel Pg antigen and found negative for DNA but strongly positive by IHC. This Pg antigen was found in neurons, astrocytes, microglial and choroid ependyma lining cells in the brain. Pull down experiments demonstrated the same protein fragments. Some aged match controls wee also positive by IHC and not Pg DNA.

Conclusion: This is the first time for this clinically relevant, unique Pg antigen to be found in many AD brain tissues. Its role in systemic inflammatory diseases for Pg is well understood and now demonstrates that its most likely source is from OMVs of oral origin.